

The cost of multiple sclerosis in Norway

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Abstract Health economic aspects have been increasingly important during introduction of new treatments for multiple sclerosis. As a partial response for Norway, a cost-of-illness study was carried out to estimate the yearly cost of the illness to society and relate costs and patients' quality of life to illness severity. Estimated cost to society was Euro 439 million in 2002 exclusive of the cost of reduced quality of life. The cost per patient was close to Euro 65,000. Account taken of methodological differences, the results compare to results for Sweden, Norway's closest neighboring country. The illness reduced patients' quality of life with 0.26. More patients were early retired because of their MS in Norway than in any of nine other European countries comprised by a recent European study, illustrating a liberal practice in Norway. The Norwegian cost of unpaid assistance was almost identical to the Swedish cost that was the lowest found across the countries in the European study. When related to illness severity, the cost per patient increased, and the patients' experienced quality of life decreased with increasing EDSS levels in line with what has been found for other countries. Cost-of-MS studies have been carried out for a number of countries.

Together they contribute to our understanding of the economic consequences of multiple sclerosis and, if their results are related to illness severity, also provide valuable information for further economic analyses of treatment and medication. Our study adds to this.

Keywords Multiple sclerosis · Cost-of-illness · Quality of life · Relapse · EDSS · Norway

JEL Classification I 18 · H 51

Introduction

Multiple sclerosis (MS) is a complex, chronic inflammatory disease of the central nervous system, characterized by demyelination and axonal loss resulting in the accumulation of neurological functional impairment and disability. The progressive loss of function results in a high level of disability [1, 2], and it has long been recognized that the illness brings high costs upon both patients and society [3–5]. During the 1990s, immunomodulatory drugs were introduced. The treatment does not cure the illness, but may delay disease progression and reduce at least some costs related to disease activity and progression [6, 7]. The medication is costly, the effect modest and health authorities are increasingly considering economics in the introduction of such treatments.

Objective

The objective of this work was to estimate of the cost of MS to the Norwegian society and the per-patient costs and patients' quality of life related to illness severity.

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Method

Cost-of-illness analyses are prevalence- or incidence-based or a combination. Prevalence-based studies give the cost of all cases in a given, usually one-year, time period. Incidence-based studies give an estimation of life-time costs for patients contracting the illness during a given time period. We used the prevalence approach, estimating the total cost of the illness during 2002. All costs to the Norwegian society were included irrespectively of who paid, and opportunity costs exclusive of taxes or subsidies were applied. Collection of data was “top-down”, using aggregate figures related to diagnoses codes from available databases, national statistics and registries, and “bottom up” collecting information directly for a limited sample of patients. Only costs caused by the patients’ MS were included, not all costs of patients with MS. Bottom-up information on resource use, work participation and quality of life was collected through a postal questionnaire survey among MS patients in Hordaland County, Western Norway.

We used an adapted version of a questionnaire that had been used in the earlier studies of MS in Europe [8, 9] to minimize problems for the patients to understand and answer the questionnaire correctly. The questionnaire was focused on the current situation the preceding month of data collection, except for questions on adaptations and special equipment that are typically provided to MS patients only once or a few times during their illness where a one-year recall period was used. Patients were explicitly asked to include only aspects related to multiple sclerosis. Quality-of-life (QoL) data were collected using a generic, preference-based instrument, the EQ-5D questionnaire [10] that was incorporated in our questionnaire.

All returned questionnaires were reviewed by the first author. Inconsistent or illogical answers were corrected where possible or else considered unanswered. A maximum number of 12 h of daily assistance from family and friends was allowed for. In cases where volume lacked for indicated resource use or reduced work participation, average volumes for the answering patients were used. All answers were entered into an Excel sheet for summation and calculation of averages. All entries were double-checked by the first author. Selected information was transferred to SPSS (Statistical Package for Social Sciences) for further analysis.

Bottom-up information on illness severity, expressed by scoring of the Kurtzke Expanded Disability Status Scale (EDSS) [11], was collected from medical records at Haukeland University Hospital, Hordaland County. EDSS is the most commonly used disability status scale in MS research and includes eight functioning systems: Pyramidal function, cerebellar function, brainstem function, sensory

function, bladder/bowel function, visual function and mental function. To measure impairment, we used a ten-point scale that divides EDSS between points 1 and 10 (10 = dead due to MS). The medical records from all MS patients were scrutinized for clinical information within 1 year by an experienced clinical neurologist.

Top-down information on resource use and work participation was collected from national registries etc. where relevant information could be extracted based on diagnoses codes or otherwise. In cases where extraction was not made by routine, we met with the registries to discuss how information could be extracted to best fit our needs and then placed an order for the information.

For *unit costs* of resource use, we would ideally have used market prices, normally reflecting the cost to society directly. In Norway, most health services are, wholly or partly, paid for by the State and pure market prices may seldom be found. Instead, maximum prices that the providers are allowed to charge for their services if the State is to pay their specified part of the price are negotiated between the Norwegian health authorities and the health service providers’ organizations. As these prices are accepted by the providers, they must be assumed to cover the full cost of the services including profit/cost of capital and therefore also reflect cost to society. As an alternative to using market prices, we therefore chose to use price or tariff lists that expressed these negotiated amounts as unit costs. For unit costs of changes in work participation, national statistics on the cost of labor was used. This contains all elements of the payment for labor and therefore reflects costs to society of utilizing the labor force.

For maximum coverage of costs, no relevant cost item was excluded from the study on *a priori* assumptions that it would be of a so modest magnitude that the cost of checking it further would not be reflected in a corresponding increase in the value of the study’s results [12].

Extrapolation of costs to society

A recent epidemiological survey showed a prevalence of about 150 per 100,000 population in Hordaland County [13]. Other recent updates of MS epidemiology in Norway have indicated prevalence at 150–160 per 100,000 population in the counties of Nord-Trøndelag and Oslo [14]. The prevalence in the three northernmost counties is usually considered to be somewhat lower, and for estimation of the total Norwegian MS population, we used a prevalence of 100/100,000 for the three northernmost counties and 150/100,000 for counties further south. In line with this, we based our extrapolation of the information from the postal survey among MS patients in Hordaland County

on the assumption of a similar MS population throughout Norway of a total of 6,750 patients.

Material

Top-down information on resource use and work participation was collected from four sources: the National Insurance Administration, the Norwegian Patient Registry, Statistics Norway and statistics from the pharmaceutical product producers.

- *The National Insurance Administration* manages disability pensions and sickness benefit in Norway and pays for occupational rehabilitation and technical aids.
- *The Norwegian Patient Registry* contains information on all patients waiting for or having received specialist health services in Norway.
- *Statistics Norway* is the central body responsible for covering the need for statistics on the Norwegian society.
- *Pharmaceutical product producers* keep track of drug sales in Norway.

Bottom-up information on resource use, work participation and quality of life was collected through the postal survey in Hordaland County. Five hundred and sixty-five patients with a definite MS diagnosis according to the Poser criteria [15] were registered in Hordaland County. In collaboration with the local MS Society, 526 (93%) of the patients were found available for the postal survey. The rest was considered unavailable either because their current postal address was unknown or due to fear that they might react negatively to be addressed as “MS patients” for the purpose of a survey. Of the 526 patients who were mailed a questionnaire, 423 (80%) responded. The questionnaire was structured into 7 different components, demographic and clinical information, drug use, ambulatory care, institutionalization, support and assistance, work participation and quality of life, and provided a broad set of information. Not only information that could not be gathered from the national-level sources described above, but also information that was also collected from those sources. This provided us with two sets of information on some important elements of resource use and work participation. Medical records at Haukeland University Hospital provided information on patient demographics, diagnoses, illness duration and disability.

Five price or tariff lists expressing negotiated amounts assumed to reflect unit costs to society were found:

- “*The standard tariff for physicians in private practice*”, “*Directions for benefits covering expenses to investigation and treatment by psychologists*” and “*Tariff for*

treatment by physiotherapists” contain the negotiated maximum prices physicians in private practice, psychologists and physiotherapists are allowed to charge for their services.

- “*Tariff for services provided by physicians in hospitals*” contains the maximum amounts hospitals are allowed to charge directly to patients. The amounts are assumed to cover approximately 50% of the hospitals’ total costs of providing the services and must be multiplied by a factor of two to reflect relevant costs to society.
- “*The Norwegian Pharmaceutical Product Compendium*” contains maximum allowed prices for drugs sold in Norway. Norwegian health authorities set the rules for the pricing and these are accepted by the producers.

In addition to information from these sources, information on unit costs was also collected from “Samdata” and Statistics Norway.

- “*Samdata*” is an organizational unit, established to produce effective management control information for Norwegian hospitals. Part of this information is average full costs at Norwegian hospitals for different stays. These average full costs must be assumed to reflect the costs to society of the stays reasonably well.
- *Statistics Norway’s* labor cost statistics reflect the prices of labor in Norway as set by the market.

The study was approved by the Norwegian Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate.

Information use

In line with the considerations above on input information availability, we used the sales figures for interferon β and glatiramer acetate from the producers’ sales statistics as our estimate of the cost to society of the use of these drugs in MS treatment. The drugs were not used for other purposes. For other prescription drugs, information on use was taken from the postal survey and on unit costs from the Norwegian Pharmaceutical Product Compendium. Average costs per month were calculated based on average unit price and recommended dose. In the case of over-the-counter drugs and complementary and alternative medication where no standard value components were available, patients’ information on monetary outlays from the survey was used.

Information on the utilization of ambulatory care was taken from the postal survey and on unit costs from the negotiated price-/tariff lists for services provided by physicians, psychologists and physiotherapists. For services provided by physicians in hospitals, the listed amounts

were multiplied by a factor of two. Price or tariff lists for services provided by other professionals were not available, and their unit costs were assumed identical to physiotherapy cost, except for the cost of visits to or by nurses were information on nurses' salaries, typical health-sector overhead costs and duration of visits were used. Transportation costs were added for all home visits.

Institutionalization of MS patients includes three forms, stays at hospitals, nursing homes and rehabilitation centers. The hospital stays are either overnight stays denoted "bed-days" or stays only during daytime, denoted "day-stays" in this study. Information on the number of bed-days and day-stays in hospitals was collected both through the postal survey in Hordaland County and the Norwegian Patient Registry. The information from the postal survey indicated a total number of bed-days and day-stays 50% higher than what was recorded at the patient registry. A comparison of the answers to the postal survey with information from medical records at Haukeland University Hospital revealed that approximately 15% of the days in hospitals reported by the patients through the survey were for earlier periods than the preceding month of data collection. This may explain slightly less than 50% of the difference in the number of days reported by the patients and the patient registry. In addition, investigation by the Norwegian Patient Registry had previously revealed that the coding in reports from the hospitals to the registry on diagnoses and medical procedures had been inaccurate. Errors were found in as much as 200 out of a random sample of 500 reports, and our own check of medical records at Haukeland University Hospital indicated specifically that also some MS-related stays had not been reported correctly. Given this uncertainty in the information from both sources, we chose our estimates mid-way between the information from the two sources. The practical consequences of possible mistakes in this choice are limited since days in hospitals counted for less than 10% of the days in hospitals, nursing homes and rehabilitation centers altogether. The unit cost of MS patients' bed-days in hospitals was estimated from information from Samdata. Corresponding information on the cost of day-stays was not available, and the unit cost of day-stays was assumed to be one-third of the cost of bed-days. We assumed MS-caused stays in nursing homes and rehabilitation centers to be bed-days only, and information on their numbers was taken from the postal survey. No specific information on the unit costs of these stays was found. We based our estimates on information given by managers of such institutions that was reasonably consistent with information in a prospect on the building and running of new institutions.

Collecting information on the cost to the Norwegian society of adaptations for and special equipment to MS patients posed special problems. Much of the equipment

and adaptations are long lasting and typically provided to patients only once, or a few times. This makes information on the volumes of the equipment and adaptations gathered through a prevalence-based questionnaire to a limited sample, especially uncertain. Further, the equipment and adaptations are often tailor-made with no general market price or unit cost. Ideally, the needed information should have been collected from the National Insurance Administration that has general responsibility to provide all Norwegian citizens with health-related needs for technical aids and buys these from commercial actors. If the purchases to MS patients could have been singled out, the total amount would have been pretty close to the total cost to society of equipment and adaptations due to MS. As for today, the National Insurance Administration's purchases are not recorded according to diagnoses, so singling out the relevant entities was not possible. Neither could the insurance administration help in providing the average costs for relevant categories of equipment, as "electric wheelchairs", "adaptations of cars" etc. We had to rely on less satisfactory sources. Information on volumes was taken from the survey, where patients were asked to supply information on the number of units they had received the last year within assumed relevant categories of equipment and adaptations. We also made an attempt to collect the information through an incidence-based approach where persons with assumed expert knowledge were asked to estimate the life-time needs of adaptations and equipment of an average MS patient. The response was close to nil, the non-responders arguing that the question could not be answered realistically. Information on unit costs were sought from suppliers and compared to stipulated unit costs within the same categories of equipment and adaptations in the Swedish study from 2001. For most of the equipment and adaptations, we found that a reasonable estimate of Norwegian (NOK)-unit costs might be the SEK costs in the Swedish study multiplied by a factor of 1.5. In one instance, adaptations of cars, we assumed that the adaptations contained more than was assumed for the Swedish study and our cost estimate was more than 6 times higher. For "other adaptation of houses", the opposite was the case and our NOK estimate was slightly lower than the Swedish SEK estimate. In a few instances, the content of the categories used in the two studies varied somewhat. This was only for equipment that from a cost perspective was unimportant, however. Information on MS patients use of paid assistance was taken from the postal survey and on unit costs from Statistics Norway's labor cost statistics for the actual occupational groups.

The cost to society of on non-paid assistance to MS patients by relatives and friends at times when the providers would alternatively have performed paid work was estimated using the human capital method. Volume

information arrived from the postal survey. Unit costs were taken from Statistics Norway's labor cost statistics. This information from statistics Norway showed that women perform fewer hours of paid work and have lower salaries than men. For our study, we assumed that these differences were not caused by differences in productivity, but by women performing more unpaid work at home. To arrive at our estimates of the unit costs, we therefore chose Statistics Norway's labor costs (gross salary including employers' contribution) for men as unit cost of help provided also by women. Assistance at times the providers alternatively would have used for leisure activities was valued at employees' salary net of tax, reflecting the providers opportunity cost of this assistance.

Also the cost to society of patients' reduced work participation was calculated using the human capital method. Information on reduced participation in paid work for the patients in the form of short- and long-term sick leaves, early retirement and reduced posts was available from the National Insurance Administration and the postal survey. The information from the National Insurance Administration indicated 30–40% more work-days lost because of sick leave due to MS than the information from the survey; 40% of the responders to the postal survey did not answer the questions on sick leave. These were assumed not to have had sick leave, and this may have resulted in some understatement of the volume of sick leaves in the information from the survey. Further, the information from the National Insurance Administration was on compensation for lost income for absences from work and had to be adjusted to be comparable to the information from the postal survey. This may have added extra uncertainty, and there were also uncertainties due to coding practices. We used our best judgment to choose our estimate somewhat closer to the information from the National Insurance Administration. As for hospitalization, the practical consequences of possible mistakes in this choice is limited since the cost of sick leaves only contributed with slightly more than 10% of the total cost of sick leaves, rehabilitation stays and reduced posts/early retirement altogether. To arrive at the number of work-years lost due to reduced posts and early retirement, we used information from the survey. The information was consistent with corresponding information from the insurance administration. For unit costs, gross salary for men including employers' contribution was used.

Information on premature deaths was available from Statistics Norway. Consistent with our prevalence approach, the number of work-years lost due to MS-caused premature deaths was estimated from Statistics Norway's "Causes of death" statistics by extracting the persons that in 2002 would have been alive at less than pension age if they had not died of MS earlier. Gross salary for men was used as estimate of unit cost to society.

Patients' answers to the EQ-5D questionnaire were, consistent with general EuroQol recommendations [16], translated into utilities via a value set originally developed with the instrument from an UK population as no comprehensive value set for Norway existed. When negative utility values occurred, these were put to zero. The number of quality-adjusted life-years (life-years at full health/QALYs) lost due to MS was estimated by calculating the difference in utility between the MS sample in our study and an age-matched general population sample [17] of same size.

The information on patients' EDSS levels from the medical records was used for two purposes. First to relate resource use, reductions in work participation and quality of life to illness severity for the group of patients responding to the postal survey and second to assign costs and quality-of-life information to non-responding and non-available patients for calculation of averages for the total MS population in Hordaland County. Of the 526 patients who were mailed a questionnaire, 423 (80%) responded. Information on the patients in the non-available and non-responding groups in the records was comparable to the responding group what age at diagnosis, gender and disease course was concerned. For the non-responding patients, also the EDSS levels compared. For the non-available patients, the average EDSS level was somewhat lower, 3.5 versus 4.3 for the responding and non-responding groups. Average costs for the responders at each EDSS level were assigned to the non-responding and non-available patients at corresponding EDSS levels.

The cost of a relapse was estimated to account for two times the difference in average monthly costs between patients at EDSS levels less than 6 with and without relapse, assuming an average relapse lasting 2 months and that relapses are seldom and difficult to identify at higher EDSS levels than 5.5. In addition, we estimated the effect of relapses on patients' quality of life by comparing quality of life in patients at EDSS levels less than 6 experiencing a relapse to that of patients on the same EDSS levels without relapse.

Results

Patient demographics

Out of 565 registered MS patients with a definite MS diagnosis in Hordaland County, 526 were considered available for a postal survey and 423 responded. The mean age at diagnosis was 37.7 (± 10.6) years, and mean EDSS-level was 4.3 (± 2.1). 65.1% was women; 25.5% indicated that they had a relapsing–remitting MS (RRMS) and 52.1% a primary or secondary progressive disease (PPMS/SPMS)

Table 1 Clinical and demographics of the responding MS patients (*n* = 423)

Characteristics	Proportion or mean (\pm SD)
Gender	
Male	34.9%
Female	65.1%
Mean age at diagnosis ^a	37.7 (\pm 10.6) years
Type of MS ^a	
Relapsing–remitting MS (RRMS)	25.5%
Progressive MS (PPMS/SPMS)	52.1%
Unknown	22.4%
Disability level ^b	
Mean EDSS level	4.3 (\pm 2.1)
Median EDSS level	4.0
EDSS score 0–3	43.5%
EDSS score 4–6.5	43.0%
EDSS score 7–9	13.5%
Relapse during last month ^a	
Yes	11.8%
No	76.2%
Unknown	12.0%
Employment	
Yes	33.7%
No	65.5%
Unknown	0.8

^a Self-reported^b Hospital records

while the rest were either uncertain or did not answer this question. Clinical and demographic data are summarized in Table 1.

Direct economic cost

Drug cost was € 30.1 million (Table 2). During 2002, the proportion of patients that used immunomodulatory treatment in Norway was approximately 25% and the cost was € 25.3 million. A total of 37% of the patients had bought other prescribed or over-the-counter drugs and 24% complementary or alternative medication the preceding month of data collection.

The cost of ambulatory care was € 24.0 million (Table 2). Nearly 20% of the patients had received ambulatory care by a neurologist the month preceding data collection and slightly more than 20% by their general practitioner. Approximately 11% had received home service by a nurse and close to 40% physiotherapy. Most patients had also received treatment from other professionals, such as occupational therapists, opticians, chiroprodists and acupuncturists. The main cost was related to nurse home visits (including transportation costs) to the

most disabled patients. Treatment by physiotherapists constituted the second largest cost item.

The cost of institutionalization was € 44.4 million (Table 4). The proportion of patients that reported they had been hospitalized (bed-days) the preceding month of data collection was 2.8%. Also 2.8% received rehabilitation and 4.0% were at nursing homes. Even with some uncertainties in the information on hospital stays, the major cost elements were related to stays at rehabilitation centers and nursing homes due to longer stays.

The cost of adaptations, equipment and assistance was € 72.9 million (Table 4). Adaptations in the home had been done during the last year in 11.3% of the patients, and 6.1% had received adaptation or support for their car. The major equipment costs were related to electric wheelchairs and adaptation of cars. We divided assistance into paid and unpaid assistance. The major costs of paid assistance were related to personal assistant, home care services and child care. The cost of unpaid assistance was related to sick leave or reduced posts for relatives, as well as spare time used by relatives and friends to help patients. Patients' transport cost was negative due to reduced travel to work.

Indirect economic cost

Patients' MS-related reduced participation in paid work was due to short-term sick leave because of acute disease activity or long-term sick leave due to disease progression, stays at rehabilitation centers, reduced posts, early retirement and premature death. The major cost components were due to early retirement and reduced posts (Table 3). Fifty percent of the responders were fully retired due to their MS. Fourteen percent had reduced posts. For these, the average reduction in work load was 51.5%.

Quality of life

Measured with the EQ-5D questionnaire using the UK value set, the patients reported a mean reduction in quality of life of 0.427. The reduction due to MS was 0.260. When measured with the EQ VAS, the reductions in quality of life were lower, mainly due to some patients at EDSS 6 and higher reporting considerably higher quality of life on the EQ VAS than what was calculated using the EQ-5D questionnaire (Table 6). The mean total reduction as measured by the EQ VAS was 0.372 and the reduction due to MS 0.205.

Cost to society

Adding the direct and indirect economic costs showed an estimated total cost of MS to the Norwegian society of €

Table 2 Estimates of the annual (2002) cost of drug use and ambulatory care due to MS

Drugs		Doses	Unit cost (€)	Annual cost (1,000 €)
Immunomodulatory drugs interferon beta/glatiramer acetate		NA	NA	25,266.3
Relapse treatment (methylprednisolone, prednisolone)		1,346	111.6	150.2
Other prescription or over-the-counter drugs		NA	NA	3,699.0
Complimentary or alternative medicine		NA	NA	1,019.9
Drug total				30,135.4
Ambulatory care	Consultations/treatments			Annual cost (1,000 €)
Physicians				2024.2
Physicians in private practice				
General practitioners	17,801	45.8	815.3	
Specialists	3,777	43.4	163.9	
Home visits	2,160	102.8	222.0	
Contact by telephone etc.	7,554	4.7	35.5	
Physicians in hospitals	9,686	81.3	87.5	
Nurses				13,896.1
At office	11,331	22.6	256.1	
Home visits	318,263	42.6	13,558.0	
Contact by telephone etc.	10,789	7.6	82.0	
Other professionals				8,041.5
Psychologists	3,777	51.4	194.1	
Physiotherapists	156,434	39.9	6,241.7	
Occupational therapists	7,554	39.9	301.4	
Incontinence advisors	1,075	39.9	42.9	
Speech therapists	1,075	39.9	42.9	
Social welfare workers	542	39.9	21.6	
Social workers	2,160	39.9	86.2	
Opticians	5,394	39.9	215.2	
Chiropodist	7,554	39.9	301.4	
Acupuncturists	8,958	39.9	357.4	
Homeopaths	1,617	39.9	64.5	
Chiropractors	542	39.9	21.6	
Healers	1,075	39.9	42.9	
Sone therapists	542	39.9	21.6	
Various other professionals	2,160	39.9	86.2	
Ambulatory care total	581,820			23,961.8

439 million during 2002 (Table 4). Direct economic costs accounted for 39% and indirect economic costs for 61%.

According to the postal survey, 14.3% of the patients at EDSS-levels 5.5 or lower had experienced a relapse the preceding month of data collection. QoL was reduced with 0.16 among the patients experiencing a relapse compared to those without relapse. Assuming a relapse lasts for 2 months on average, a relapse was estimated to cost € 5,170 (Table 5).

Analyses of costs and quality of life related to illness severity showed increasing MS-related costs and reduced

quality of life along with increasing disability (Table 6) in line with what have been found for other countries [18]. Direct economic costs related to treatment and care of MS patients were more than 7 times higher at EDSS-levels 7–8 compared to levels 1–2, and indirect economic costs due to patients' reduced participation in paid work were more than 2 times higher. The relatively modest increase in indirect economic costs is mainly explained by a large part of the patients at EDSS-levels 1–2 having reduced posts, in addition to some also being fully retired already at these low levels of illness severity.

Table 3 Estimates of the annual (2002) cost of patients' reduced work participation

Patients reduced work participation due to	Duration	Unit cost (€)	Annual cost (€ 1,000)
Sick leave			27,337.6
Women	76,112 days	236.8	18,023.3
Men	39,334 days	236.8	9,314.3
Rehabilitation			4,468.7
Women	12,404 days	236.8	2,937.3
Men	6,467 days	236.8	1,531.4
Reduced post/early retirement			207,314.1
Women	2,758 years	54,327.6	149,835.5
Men	1,058 years	54,327.6	57,478.6
Premature death due to MS ^a	524 years	54,327.6	28,467.7
Patients reduced work participation, total			267,588.1

^a Statistics Norway: causes of death

Table 4 Estimate of the 2002 cost of MS to the Norwegian society (€ 1,000)

Direct economic cost	171,387
Drugs	30,135
Ambulatory care	23,962
Institutionalization	44,430
Adaptations and equipment	27,754
Paid assistance	11,983
Unpaid assistance	33,123
Indirect economic cost	
Patients' reduced work participation	267,588
Total	438,975

Table 5 Cost of a MS relapse during 2002 (€)

Cost category	Patients with relapse per month	Patients without relapse per month	Difference × 2 = cost of a relapse
Direct economic cost	2,935	1,570	2,730
Indirect economic cost	3,686	2,466	2,440
Total economic cost	6,621	4,036	5,170

Discussion

The objective of this study has been to estimate the total annual cost of MS to the Norwegian society and the per-patient costs and patients' quality of life related to illness severity. Our estimate of the cost to society for 2002 was €

439 and per patient € 65,037. Our approach was prevalence based, giving MS-caused costs during 2002. Prevalence-based approaches are usually considered suitable for chronic illnesses like MS. Incidence-based approaches require the estimation of life-time costs for patients contracting the illness. This is virtually impossible for MS due to the complexity and long duration of the illness. We used the human capital method to estimate the cost to society of all reduced work participation. It has been argued that this may lead to an overstatement of this cost. First, because labor costs includes the production of health-related goods and services [19]. Second because, particularly in times of high unemployment, a worker might be rapidly replaced and hence no production loss would occur [20] and third, especially for premature deaths also because reduced consumption is not taken into account [21]. These issues are debated and it is not clear how adjustments might be done correctly. On balance, we chose, in line with the choice that has been most typically made also in other cost-of-MS studies, not to do any such adjustments.

In a study for Sweden [22] Norway's closest neighboring country, the cost per patient was estimated to € 53,601 in 2005, 17.6% less than the Norwegian estimate for 2002. Norwegian price-level increases were marginal from 2002 to 2005, so the nominal amounts should be comparable. More than half of the difference is due to two methodological choices, made differently for the studies. The cost of premature death was included in the Norwegian estimate but not in the Swedish. This accounts for 37% of the difference. Further, in the Norwegian study, equal productivity for both sexes was assumed for the calculation of the cost of reduced work participation while gender-specific productivity was used for the Swedish study. This accounts for another 24%. The remaining difference is caused by a combination higher costs of patients' reduced participation in paid work, institutionalization, ambulatory care and equipment and adaptations in the Norwegian study, and lower costs of paid assistance and drugs. The Norwegian cost of patients' reduced participation in paid work was 90% higher than in the Swedish study. One-third of this is due to the cost of MS patients working in reduced posts being included in the Norwegian study but not in the Swedish. The remaining difference is mainly due to full-time early retirement being more than 40% higher in Norway than in Sweden (51.0/35.7%). It was also higher than in any other country in a study of 9 European countries including Sweden [23], illustrating a liberal practice in Norway. The cost of paid assistance was close to 10 times higher in Sweden than in Norway almost exclusively due to much more intensive use of personal assistants. The Norwegian cost of institutionalization exceeded the Swedish by 21% due to significantly more days in institutions but on average somewhat lower unit costs, and the Norwegian

Table 6 Average quality of life and annual (2002) cost per patient (1,000 €) at categorized EDSS levels (1–9)

Quality of life	Categorized EDSS levels								
	1	2	3	4	5	6	7	8	9
Generated by the									
EQ-5D descriptive system	.800	.757	.701	.617	.536	.443	.211	.142	.056
EQ VAS	.782	.751	.673	.606	.574	.513	.530	.379	n.a.
Per patient costs									
Direct economic cost	7.8	11.4	19.8	24.3	47.9	53.3	50.6	92.4	129.2
Indirect economic cost	22.2	22.1	33.9	37.3	48.7	41.9	45.8	52.1	54.3
Total economic cost	30.0	33.5	53.7	61.6	96.6	95.2	96.4	144.5	183.5

cost of ambulatory care exceeded the Swedish by 18%, mainly due to more extensive use. The Norwegian drug cost was 31% lower than the Swedish mainly due to more use of DMDs in Sweden in 2005 than in Norway in 2002. Finally, the Norwegian cost of equipment and adaptations exceeded the Swedish by as much as 300%. It is especially difficult, however, to get precise information on resource use and unit costs in this area. The cost of unpaid assistance in Norway was almost identical to the Swedish cost that was the lowest found across the nine countries in the European study.

To provide a complete assessment of the burden of an illness, intangible costs due to pain, grief, anxiety and social handicap should theoretically also be included in the calculations [19]. However, due to difficulties in quantifying these items, they are often excluded from cost-of-illness studies [22]. In the Swedish study, the costs were approximated, though, by relating estimated utility losses to a threshold value for a QALY gained of approximately € 50,000 implied by reimbursement decisions for new treatments in selected countries [23] and therefore also assumed to indicate society's willingness to pay for such gains [24], indicating an intangible cost of € 11,400 per patient and year. Applying the same approximation to our Norwegian data would have resulted in an additional cost per patient of approximately € 13,000 and € 88 million for society.

At the outset, we planned to use top-down information to a largest possible degree, expecting this to be complete and of high quality. Closer investigation, however, revealed large uncertainties in the information.

A wide specter of information for our study was gathered through the postal survey in Hordaland County, and one potential limitation of this information and our further extrapolations of it should be noted. The cost effects of the illness to society for the patients in the MS population in Hordaland County may not be representative for the corresponding cost effects in other parts of Norway. The Norwegian Multiple Sclerosis Competence centre is located

at the Department of Neurology, Haukeland University Hospital in Hordaland County, and numerous MS studies conducted at the department may increase the contact frequency of the patients to the department. However, epidemiological studies from Hordaland have shown similar prevalence and patient characteristics of the MS population compared to other parts of the country [13]. In addition, national surveys of the use of immunomodulatory treatments have shown that treatment frequency in Hordaland County has been on the average for the whole county [14]. Hordaland County also comprises both rural and urban areas like most other counties in Norway and contains approximately 10% of the MS patients in the country. This should contribute to make the MS population in Hordaland County reasonably representative for the national population. The possible effect of eventual non-representativeness of our chosen survey population might therefore be expected to be modest. For the comparisons with the Swedish study, it should be noted the average EDSS level for our sample was 0.8 lower than for the Swedish (4.3/5.1). This might have reduced the comparability of the results. Estimates of patients' EDSS levels are inherently uncertain, however, and the information was collected differently for the studies, assessed from medical records for the Norwegian study, and self-reported for the Swedish. For these reasons, this point has been left out of the discussion.

When we related costs per patient and patients' quality of life to illness severity, the per-patient cost increased and patients' quality of life decreased with increasing illness severity in line with what has been found for other countries when applying the UK value set to our patients' reported EQ-5D health states. There is not one value set that is unequivocally "the best" for a given study. Another value set that might have been relevant for our study could be a European value set, constructed from data from 11 valuation studies in 6 European countries [16]. Applying this value set gave quality-of-life values that deviated from the values calculated from the UK value set with less than 5% for patients up to EDSS-level 5 and with 7% for EDSS-

level 6, but considerably more for EDSS-levels 7, 8 and 9. The deviations were in both directions. Close to the same pattern is found if the quality-of-life values calculated from the UK value set, are compared with the QoL measured by the EQ VAS, deviations of less than 5% up to EDSS-level 4, deviations of 6 and 16% at EDSS-levels 5 and 6 respectively, and considerably larger deviations for higher EDSS levels, indicating larger uncertainty in the measurement of quality of life for the most seriously ill MS patients.

Cost-of-MS-studies have been carried out for a number of countries. Their results have varied widely, due to differences in their approach to data collection, the type of resources included, the valuation of the resources, the type of patients concerned, the sample process and the quality of the analysis, in addition to differences between the countries in absolute and relative prices and healthcare and social organization [25]. It is hence inappropriate to directly compare the studies and costs. Still, together they contribute to increase our understanding of the economic consequences of multiple sclerosis and, if their results are related to illness severity, also provide valuable information for further economic analyses of treatment and medication. Our study adds to this. In Norway, internationally acknowledged guidelines (NICE) are the basis for admittance and treatment of MS patients. This contributes to make our findings relevant to other countries. Further, residents of Norway are universally covered by the welfare system and thus having equal financial access to diagnostic procedures and health care, giving our study validity.

Conclusion

We estimated the cost of MS to the Norwegian society to € 439 million in 2002. Per patient cost was close to € 65,000. The results compare to results from a study in Sweden, Norway's closest neighboring country. When costs per patient and the patients' quality of life were related to illness severity, the costs per patient increased and quality of life decreased with increasing EDSS levels in line with what has been found for other countries. Studies that relate per-patient MS costs and patient's quality of life to illness severity have been carried out for a number of countries. They provide valuable information for economic analyses of treatment and medication. Our study adds to this.

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